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Immunosuppression and Alterations of T-Lymphocyte Subpopulations After Rubella Vaccination

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Lymphocyte stimulation tests and determination of T-lymphocyte subpopulations were undertaken in 11 subjects before and after rubella vaccination and in 11 controls. The lymphocyte stimulation response to phytohemagglutinin was suppressed 7 to 10 days after vaccination. The proportion of T lymphocytes with receptors for the Fc part of immunoglobulin G increased after vaccination, whereas there was no significant change in the proportion of T lymphocytes with immunoglobulin M-Fc receptors.

Cell-mediated immune reactions such as delayed dermal hypersensitivity and in vitro lymphocyte stimulation are often depressed during various viral diseases such as morbilli, rubella, and infectious mononucleosis (4, 6, 8, 12, 13, 15, 24).

This depression of cell-mediated immunity (CMI) might be the result of activation of cells with suppressor function. In mice it has been shown that a subpopulation of T lymphocytes with specific surface antigens acts as suppressor cells (for review, see reference 25).

Recently Moretta et al. have identified subsets of human T cells that have receptors for the Fc portion of either immunoglobulin G (IgG) (T_G cells) or IgM (T_M cells) or that lack these receptors (5, 18). It has been shown that T_G cells have a suppressor effect, whereas T_M cells have a helper effect on pokeweed mitogen-induced or antigen-specific B-cell responses in vitro (9, 19).

In the present study we have investigated whether the suppression of CMI, occurring during viral infection, is correlated to any changes in the size of the T-lymphocyte subpopulations. We chose to study infection with an attenuated rubella vaccine since it has been shown that CMI is depressed the same way after vaccination as during natural rubella infection (4, 7, 16, 17, 23).

MATERIALS AND METHODS

Heparinized blood was obtained from 11 female nursing students 17 to 39 years old before and at various intervals after vaccination with live, attenuated rubella vaccine (Wistar RA 27/3 lot RB 25/19 and RB 25/20; The Wellcome Foundation Ltd., London). Before vaccination, all the vaccinees were shown to be seronegative to rubella by hemolysis in gel technique (no detectable zon) (22). Eleven unvaccinated seropositive nursing students 17 to 39 years old served as controls and were tested at the same intervals as the vaccinees.

Leukocyte counts and differential counts were always done in connection with the drawing of blood for lymphocyte separation.

Cell preparation. The heparinized blood was diluted 1:2 in 0.9% saline, layered on ficoll-isopaque (Ficoll-Paque, Pharmacia, Uppsala, Sweden) and centrifuged at 400 × *g* for 40 min. The interphase cells were collected and washed twice in phosphate-buffered saline without calcium and magnesium and once in RPMI 1640 medium (Gibco Bio-Cult, Paisley, Scotland) (1). This cell population usually contained 5 to 10% polymorphonuclear cells. A portion of this cell suspension was used for cell cultures. The remaining cells were treated with carbonyl iron (100 mg for 30 min at 37°C) after which the phagocytic cells were removed with a magnet. Cultures were also set up with phagocyte-depleted cells.

Culture conditions and assay for deoxyribonucleic acid (DNA) synthesis. Cultures for determination of DNA synthesis were set up in duplicate or triplicate in tubes containing 5×10^5 mononuclear cells in 1 ml of RPMI 1640 medium supplemented with 10% AB serum pool (treated at 56°C for 30 min), L-glutamine, penicillin, and streptomycin or in microplates (3040 Microtest II, Falcon Plastics, Oxnard, Calif.) with 2×10^5 mononuclear cells per well in 0.2 ml of the same medium as above. The cultures were incubated at 37°C in humidified air with 5% CO_2. After 0 to 4 days of incubation, 0.1 μCi of [^{14}C]thymidine (Radiochemical Centre, Amersham, England) was added to each tube and 0.05 μCi was added to each microplate well. After further incubation for 18 h the cultures were frozen. The cells were harvested on membrane filters (Millipore Corp.). Radioactivity was measured in a liquid scintillation counter and expressed in counts per minute per culture. The mean of duplicates or triplicates was calculated.

Antigens and mitogens. Cultures were stimulated with the following: (i) phytohemagglutinin (PHA) (Wellcome Research Laboratories, Beckenhan, England) at final concentrations of 0.25, 2.5, and 25 μg/ml in microplates ([^{14}C]thymidine was added after 48 h)

and (ii) purified protein derivate (PPD) (Statens Serum Institut, Copenhagen, Denmark) at final concentrations of 1 and 10 μg/ml in tubes ([^{14}C]thymidine was added after 4 days).

PHA and PPD stimulations were done by using cell cultures containing phagocytes as well as those depleted of phagocytes. To study spontaneous DNA synthesis [^{14}C]thymidine was added to some cultures on day 1.

Assay for E-rosette-forming cells (10). A total of 500,000 lymphocytes in 0.1 ml of RPMI 1640 medium was mixed with 0.1 ml of 1% neuraminidase (Behringwerke, Germany)-treated sheep erythrocytes (SRBC) in 100% heat inactivated fetal calf serum (Flow Laboratories, Irvine, England). The tubes were centrifuged at 200 × g for 5 to 6 min, incubated at room temperature for 1 h, and then placed at 4°C overnight. The cells were suspended and counted for E-rosette-forming cells. Lymphocytes binding three or more SRBC were regarded as positive. Tests were done in duplicate.

Separation of T and B lymphocytes. T cells were separated by rosetting with SRBC followed by gradient centrifugation. Lymphocytes at a concentration of 10×10^6 to 15×10^6 cells/ml in RPMI 1640 medium were mixed with equal volumes of 5% neuraminidase-treated SRBC in 100% fetal calf serum. The tubes were centrifuged, incubated at room temperature for 1 h, and then placed at 4°C overnight. Rosetting and nonrosetting cells were separated by centrifugation in a Ficoll-Isopaque gradient. Cells in the interphase were collected. The pellet was suspended, and the gradient centrifugation was repeated. The final pellet contained 95 to 100% E-rosette-forming cells. The SRBC were then lysed by treatment with 0.83% NH_4Cl.

Anti-oxRBC antibody. Anti-ox erythrocytes (oxRBC) antibodies were raised in rabbits by repeated injections intraperitoneally of 1 to 5 ml of 25% oxRBC. IgM and IgG fractions were prepared from rabbit antisera by Sephadex-G200 gel filtration. The hemagglutination titer of concentrated IgM fractions was 1/32 to 1/64 and the titer of concentrated IgG fractions was 1/128 to 1/256. Treatment with 2-mercaptoethanol completely abolished the hemagglutinating capacity of the IgM fractions but did not change the hemagglutination titer of the IgG fractions.

Preparation of oxRBC-antibody complexes. Equal volumes of washed oxRBC at a concentration of 2% and purified IgM antibody (0.5 to 0.25 HA unit) or IgG antibody (0.5 to 0.25 HA unit) were mixed and incubated at 37°C for 30 min. The ox erythrocyte-IgG antibody ($oxEA_G$) and the ox erythrocyte-IgM antibody ($oxEA_M$) complexes were then washed and resuspended to a concentration of 0.5%.

Determination of T_G and T_M cells. T_G and T_M cells were identified by rosette formation as described by Moretta and co-workers (5, 18). A 0.1-ml amount of a cell suspension containing 3×10^6 cells/ml was mixed with 0.1 ml of $oxEA_G$ or $oxEA_M$ and centrifuged at 200 × g for 5 min followed by incubation at 4°C for 30 min. The pellet was gently resuspended, and 400 lymphocytes from each tube were counted for rosette formation. A rosette was defined as a lymphocyte with three or more red cells attached. All tests were performed in duplicate. T cells examined for $oxEA_M$ rosette formation had been incubated overnight at 37°C in RPMI 1640 medium supplemented with 20% fetal calf serum. Tests for T_G cells were done by using freshly prepared T cells as well as T cells incubated overnight at 37°C.

Statistics. The differences between postvaccination and prevaccination values were calculated and analyzed by the Wilcoxon rank sum test.

RESULTS

PHA stimulation of DNA synthesis. Lymphocyte stimulation tests performed in vaccinees before and after vaccination and in unvaccinated controls showed that there was a significant decrease in the stimulation response to PHA at 0.25 μg/ml ($P < 0.02$) and 25 μg/ml ($P < 0.01$) 7 to 10 days after vaccination (Tables 1 through 3). There was a slight decrease also in the response to the optimal dose of PHA (2.5 μg/ml), but this decrease was not significant. Two vaccinees (9 and 11) and their corresponding controls responded poorly to PHA at 0.25 μg/ml when tested before vaccination. After vaccination these vaccinees did not have a decreased response; however, since the controls showed an increased response, it seems likely that the low thymidine uptake before vaccination was due to some technical error.

The PHA response was always lower in phagocyte-depleted cell cultures than in cell cultures containing phagocytes. The difference in PHA responsiveness between phagocyte-depleted cell cultures and phagocyte-containing cultures was

TABLE 1. *Lymphocyte stimulation response to PHA at 0.25 μg/ml and percentage of T_G cells in 11 vaccinees before and after vaccination*[a]

Vaccinee	Day 0		Days 7-10	
	[^{14}C]thymidine uptake (cpm × 1,000)[b]	T_G cells (%)	[^{14}C]thymidine uptake (cpm × 1,000)[b]	T_G cells (%)
1	30.7	19	5.7	27
2	23.0	16	6.5	13
3	21.8	21	15.6	37
4	19.7	4	16.8	7
5	21.5	4	23.9	7
6	10.2	33	3.3	50
7	14.6	13	5.9	18
8	15.4	13	11.0	19
9	0.5	5	1.3	14
10	9.1	10	5.8	14
11	1.3	14	1.5	25
Mean	15.3	14	8.8	21
Median	15.4	13	5.9	18

[a] T lymphocytes incubated overnight at 37°C before rosetting.

[b] cpm, counts per minute.

of the same magnitude before and after vaccination (data not shown).

PPD stimulation. The lymphocyte stimulation response to PPD was lower after vaccination than before vaccination, but the difference did not reach significance due to the great individual variation of the response (Table 4).

Spontaneous DNA synthesis. There was no change in the spontaneous DNA synthesis after vaccination (data not shown).

Blood picture. There was no significant change in the leukocyte counts after vaccination (Table 5). Differential counts showed a decrease in the proportion of lymphocytes after vaccination, but this decrease was not significant. However, when absolute values of lymphocytes were calculated there was a significant reduction after vaccination ($P < 0.01$).

E-rosettes. The proportion of E-rosettes did not change after vaccination. In the vaccinees the median was 83% (range, 78 to 90) before vaccination and 82% (range, 79 to 89) after vaccination.

Subpopulations of T lymphocytes. A total of 10 out of 11 vaccinees had a higher proportion of T_G cells 7 to 10 days after vaccination than they did before vaccination (Tables 1, 2, 6). One of the vaccinees had a T_G cell level above the normal range before vaccination but still showed a further increase in the proportion of T_G cells after vaccination. In the unvaccinated controls there were only minor changes in the T_G cell level. The increase in the percentage of T_G cells in the vaccinees is statistically significant ($P < 0.01$). The absolute number of T_G cells did not increase after vaccination since the total number of lymphocytes in the peripheral blood was reduced.

T_G cell determinations were done with fresh T cells as well as T cells which had been incubated at 37°C overnight. In both instances an increase of the T_G cell level was observed after vaccination, but the increase was significant only in the tests where incubated T cells were used. This difference was because in unvaccinated subjects (the vaccination group before vaccination and the control group) the percentage of T_G cells usually (in 14 out of 21 subjects) decreased slightly after incubation of T cells, whereas in the vaccinees the proportion of T_G cells often (in

TABLE 2. *Lymphocyte stimulation response to PHA at 0.25 μg/ml and percentage of T_G cells in 11 controls*[a]

Control	Day 0		Days 7-10	
	[^{14}C]thymidine uptake (cpm × 1,000)[b]	T_G cells (%)	[^{14}C]thymidine uptake (cpm × 1,000)[b]	T_G cells (%)
1	21.3	11	18.6	9
2	Not done	18	Not done	22
3	21.0	6	22.6	5
4	20.8	13	17.5	14
5	5.9	16	6.0	12
6	15.6	6	11.7	5
7	7.0	10	5.2	13
8	7.1	11	9.0	8
9	1.8	13	5.0	14
10	13.9	9	16.3	9
11	1.6	14	5.2	16
Mean	11.6	12	11.7	12
Median	10.5	11	10.3	12

[a] T lymphocytes incubated overnight at 37°C before rosetting.

[b] cpm, Counts per minute.

TABLE 4. *Lymphocyte stimulation response to PPD in 10 vaccinees before and 7-10 days after rubella vaccination and in 9 controls*

Vaccination day	Response[a] to PPD concn	
	1 μg/ml	10 μg/ml
Before vaccination		
Vaccinees	18.3 (5.0-44.0)	25.3 (5.9-48.7)
Controls	26.0 (6.8-50.7)	31.5 (10.6-51.0)
7-10 days after vaccination		
Vaccinees	7.1 (1.2-23.6)	11.2 (3.0-22.8)
Controls	30.0 (4.7-54.4)	27.3 (6.9-63.8)

[a] Median and (range) × 1,000 counts per minute.

TABLE 3. *Lymphocyte stimulation response to PHA in 11 vaccinees before and 7 to 10 days after rubella vaccination and in 10 controls*

Vaccination day	Response[a] to PHA concn		
	0.25 μg/ml	2.5 μg/ml	25 μg/ml
Before vaccination			
Vaccinees	15.4 (0.5-30.7)	20.7 (6.4-35.0)	15.9 (7.9-28.6)
Controls	10.5 (1.6-21.3)	18.7 (5.7-28.7)	15.7 (2.1-25.4)
7-10 days after vaccination			
Vaccinees	5.9 (1.3-23.9)	19.0 (3.7-27.8)	11.0 (4.7-24.9)
Controls	10.3 (5.0-22.6)	18.5 (11.3-28.8)	15.0 (4.9-23.2)

[a] Median and (range) × 1,000 counts per minute.

TABLE 5. *Leukocyte counts, percentage of lymphocytes, and absolute number of lymphocytes in 11 vaccinees before and 7-10 days after rubella vaccination and in 10 controls*[a]

Vaccination day	Leukocytes C × 10^9/liter	Lymphocytes (%)	Lymphocytes (absolute no. × 10^9/liter)
Before vaccination			
Vaccinees	5.9 (4.5-6.5)	36 (30-51)	2.2 (1.6-2.6)
Controls	5.3 (4.2-7.0)	40 (19-53)	2.0 (1.3-3.2)
7-10 days after vaccination			
Vaccinees	5.7 (3.2-12.8)	32 (6-40)	1.7 (0.4-2.3)
Controls	6.1 (4.3-12.5)	37 (23-53)	2.1 (1.4-6.6)

[a] Values are median and (range).

TABLE 6. *Percentages and absolute numbers of T_G cells in 11 vaccinees before and 7-10 days after rubella vaccination and in 11 controls*

Vaccination day	T_G cells (%)[a]	T_G cells (%)[b]	T_G cells, absolute no. × 10^9/liter of blood[c]
Before vaccination			
Vaccinees	15 (4-35)	13 (4-33)	0.21 (0.06-0.44)
Controls	12 (6-19)	11 (6-18)	0.18 (0.10-0.35)
7-10 days after vaccination			
Vaccinees	16 (9-41)	18 (7-50)	0.19 (0.05-0.57)
Controls	13 (5-18)	12 (5-22)	0.23 (0.11-0.31)

[a] Median (range). T_G cells determined using freshly prepared T cells.
[b] Median (range). T_G cells determined after overnight incubation of T cells at 37°C.
[c] Median range. T cells incubated.

TABLE 7. *Percentages and absolute numbers of T_M cells in 10 vaccinees before and 7-10 days after rubella vaccination and in 10 controls*[a]

Vaccination day	T_M cells (%)	T_M cells, absolute no. × 10^9/liter of blood
Before vaccination		
Vaccinees	52 (26-67)	0.86 (0.39-1.28)
Controls	51 (31-60)	0.76 (0.49-1.75)
7-10 days after vaccination		
Vaccinees	52 (17-71)	0.64 (0.18-1.10)
Controls	50 (38-74)	0.96 (0.60-3.63)

[a] Values are median and (range).

6 out of 10 cases) increased slightly after incubation of T cells.

The relative proportion of T_M cells did not change significantly after vaccination, but the absolute number was reduced ($P < 0.01$) because of the decrease of lymphocytes in the blood (Table 7).

DISCUSSION

In the present study suppression of the lymphocyte stimulation response to PHA was demonstrated 7 to 10 days after rubella vaccination. Several other investigators have previously shown suppression of various parameters of CMI after vaccination with attenuated rubella vaccines, including the vaccine strain used in the present study (4, 7, 16, 17, 23). In some of these previous studies suppression of the PHA response was most evident when suboptimal doses of PHA were used (4, 23). We found no significant suppression of the response to optimal PHA doses, but at both sub- and supraoptimal PHA concentrations there was a suppression.

It is not likely that this suppression of lymphocyte stimulation was caused by serum factors since we supplemented all lymphocyte cultures with the same pooled AB serum. In other studies suppression has also been demonstrated in the absence of autologous serum (4) or when autologous serum drawn before vaccination was used (23), although Maller and co-workers found the suppression after natural rubella infection to be more pronounced in cultures supplemented with autologous plasma than in cultures with pooled homologous plasma (13).

One possible explanation for the suppression of CMI after rubella vaccination could be that the lymphocytes had been infected with virus and that virus-infected lymphocytes are less responsive to mitogens. This hypothesis is supported by studies made by Buimovici-Klein and Cooper (3). They isolated vaccine virus from lymphocytes after rubella vaccination of seronegative persons and observed that the discovery of virus correlated in time with suppression of the PHA response. On the other hand, it has been shown previously that rubella vaccination induces approximately the same degree of immunosuppression in seropositive individuals as in seronegative individuals (23). If infection of the lymphocytes is the mechanism behind the immunosuppression, one has to postulate that the lymphocytes of immune persons also become infected after rubella vaccination, which to us seems less likely. Maller and co-workers found that when lymphocyte cultures were infected in vitro with rubella virus there was a suppression of the PHA response, but only in lymphocytes from immune donors, suggesting an immunological mechanism (14).

The transient immunosuppression that occurs in association with various acute infections might be the result of increased suppressor cell activity. Macrophages have been shown to have a suppressor effect on the lymphocyte stimulation response in patients with neoplastic diseases (for review see reference 2) and on the in vitro B-cell response in patients with tuberculosis (11). In the present study removal of phagocytic

cells did not restore the lymphocyte stimulation response to the level found before vaccination. This is in accordance with the results of a previous study in which macrophages were removed by adherence from lymphocytes of rubella-infected subjects (23).

In the present study we found an increase in the proportion of T_G cells after vaccination. It is well documented that T_G cells can act as suppressor cells on B-cell responses in vitro (9, 19). It has also been shown that T_G cells from newborns have a suppressor effect on the proliferative response of lymphocytes from the mothers (20). Thus it is possible that the suppression of the lymphocyte stimulation response seen after rubella vaccination is caused by the activation of T_G cells. To prove this it will be necessary to compare the stimulation response of lymphocyte cultures depleted of T_G cells with that of cultures containing T_G cells. An elevation of T_G cell values has also been observed in some other infections, namely influenza, viral hepatitis (L. Moretta, personal communication), and tuberculosis (11). It seems likely that an increase in the proportion of T_G cells is part of the normal immunoregulatory response in various infections.

In unvaccinated subjects the proportion of T_G cells usually decreased slightly after overnight culture of T cells, which is in agreement with a previous report (21). However, in the vaccinated subjects there was a slight increase in the proportion of T_G cells after overnight culture of the T cells. We do not know the reason for this increase.

In conclusion, we have shown that after rubella vaccination there is a suppression of the lymphocyte stimulation response and also an increase in the percentage of T_G cells. However, we have no direct proof that the T_G cells cause the immunosuppression.

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LITERATURE CITED

1. **Bøyum, A.** 1976. Isolation of lymphocytes, granulocytes and macrophages. Scand. J. Immunol. **5**(Suppl. 5):9–15.
2. **Broder, S., and T. A. Waldmann.** 1978. The suppressor-cell network in cancer (second of two parts). New Engl. J. Med. **299**:1335–1341.
3. **Buimovici-Klein, E., and L. Z. Cooper.** 1979. Immunosuppression and isolation of rubella virus from human lymphocytes after vaccination with two rubella vaccines. Infect. Immun. **25**:352–356.
4. **Buimovici-Klein, E., T. Vesikari, C. F. Santangelo, and L. Z. Cooper.** 1976. Study of the lymphocyte in vitro response to rubella antigen and phytohemagglutinin by a whole blood method. Arch. Virol. **52**:323–331.
5. **Ferrarini, M., L. Moretta, R. Abrile, and M. L. Durante.** 1975. Receptors for IgG molecules on human lymphocytes forming spontaneous rosettes with sheep red cells. Eur. J. Immunol. **5**:70–72.
6. **Finkel, A., and P. B. Dent.** 1973. Abnormalities in lymphocyte proliferation in classical and atypical measles infection. Cell. Immunol. **6**:41–48.
7. **Ganguly, R., C. L. Cusumano, and R. H. Waldman.** 1976. Suppression of cell-mediated immunity after infection with attenuated rubella virus. Infect. Immun. **13**:464–469.
8. **Haider, S., M. de L. Coutinho, R. T. D. Emond, and R. N. P. Sutton.** 1973. Tuberculin anergy and infectious mononucleosis. Lancet **ii**:74.
9. **Heijnen, C. J., F. UytdeHaag, F. H. J. Gmelig-Meyling, and R. E. Ballieux.** 1979. Localization of human antigen-specific helper and suppressor function in distinct T-cell subpopulations. Cell. Immunol. **43**:282–292.
10. **Jondal, M.** 1976. SRBC rosette formation as a human T lymphocyte marker. Scand. J. Immunol. **5**(Suppl. 5): 69–76.
11. **Katz, P., R. A. Goldstein, and A. S. Fauci.** 1979. Immunoregulation in infection caused by *Mycobacterium tuberculosis*: the presence of suppressor monocytes and the alteration of subpopulations of T lymphocytes. J. Infect. Dis. **140**:12–21.
12. **Kauffman, C. A., J. P. Phair, C. C. Linnemann, and G. M. Schiff.** 1974. Cell-mediated immunity in humans during viral infection. I. Effect of rubella on dermal hypersensitivity, phytohemagglutinin response and T lymphocyte numbers. Infect. Immun. **10**:212–215.
13. **Maller, R., A. Frydén, and L. Sörén.** 1978. Mitogen stimulation and distribution of T- and B-lymphocytes during natural rubella infection. Acta. Pathol. Microbiol. Scand. Sect. C **86**:93–98.
14. **Maller, R., and L. Sörén.** 1977. In vitro effects of rubella virus, strain RA 27/3 on human lymphocytes. I. Viral inhibition of mitogen stimulation in relation to rubella haemagglutination inhibition antibodies. Acta Pathol. Microbiol. Scand. Sect. C **85**:49–56.
15. **Mangi, R. J., J. C. Niederman, J. E. Kelleher, J. M. Dwyer, A. S. Evans, and F. S. Kantor.** 1974. Depression of cell-mediated immunity during acute infectious mononucleosis. New Engl. J. Med. **291**:1149–1153.
16. **McMorrow, L. E., T. Vesikari, S. R. Wolman, J. P. Giles, and L. Z. Cooper.** 1974. Suppression of the response of lymphocytes to phytohemagglutinin in rubella. J. Infect. Dis. **130**:464–469.
17. **Midulla, M., L. Businco, and L. Moschini.** 1972. Some effects of rubella vaccination on immunologic responsiveness. Acta Paediatr. Scand. **61**:609–611.
18. **Moretta, L., M. Ferrarini, M. L. Durante, and M. C. Mingari.** 1975. Expression of a receptor for IgM by human T cells in vitro. Eur. J. Immunol. **5**:565–569.
19. **Moretta, L., S. R. Webb, C. E. Grossi, P. M. Lydyard, and M. D. Cooper.** 1977. Functional analysis of two human T-cell subpopulations: help and suppression of B-cell responses by T-cells bearing receptors for IgM or IgG. J. Exp. Med. **146**:184–200.
20. **Oldstone, M. B. A., A. Tishon, and L. Moretta.** 1977. Active thymus derived suppressor lymphocytes in human cord blood. Nature (London) **269**:333–335.
21. **Pichler, W. J., L. Lum, and S. Broder.** 1978. Fc-receptors on human T lymphocytes. I. Transition of $T\gamma$ to $T\mu$ cells. J. Immunol. **121**:1540–1548.
22. **Skaug, K., I. Ørstavik, and J. C. Ulstrup.** 1975. Application of the passive haemolysin test for the determination of rubella virus antibodies. Acta Path. Microbiol. Scand. Sect. B **83**:367–372.

23. **Vesikari, T., and E. Buimovici-Klein.** 1975. Lymphocyte responses to rubella antigen and phytohemagglutinin after administration of the RA 27/3 strain of live attenuated rubella vaccine. Infect. Immun. **11**:748–753.
24. **Von Pirquet, C.** 1908. Das verhalten der Kutanen Tuberkulinreaction während der Masern. Dtsch. Med. Wochenschr. **34**:1297–1300.
25. **Waldmann, T. A., and S. Broder.** 1977. Suppressor cells in the regulation of the immune response. Prog. Clin. Immunol. **3**:155–199.